International Journal of Hygiene and Environmental Health 219 (2016) 233–238

Contents lists available at ScienceDirect

International Journal of Hygiene and Environmental Health

journal homepage: www.elsevier.com/locate/ijheh

Review

The relationship between environmental relative moldiness index values and asthma

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ARTICLE INFO

Article history:
Received 30 October 2015
Received in revised form 26 January 2016
Accepted 27 January 2016

Keywords:
Mold
ERMI
Asthma
Area under the curve
Logistic regression

ABSTRACT

Indoor mold exposures have been qualitatively linked to asthma for more than 25 years. Our goal has been to turn this qualitative link into a quantitative assessment of asthma risk from mold exposures as estimated by the home's environmental relative moldiness index (ERMI) value. The home's ERMI value is derived from the quantitative PCR analysis of 36 molds in a dust sample. Six epidemiological studies of the relationship between ERMI values and asthma, in cities across the U.S., showed that both children and adults with asthma were living in homes with significantly higher ERMI values than the control or comparison homes. Based on these six studies, the accuracy of the ERMI value's link to occupant asthma was analyzed using receiver operating characteristic (ROC) curve and area under the curve (AUC) statistical analysis. The AUC was 0.69 which places the test accuracy in the "fair to good" range for a medical diagnostic test. A logistic regression analysis of the six studies was performed to generate an equation that can be used to predict occupant asthma at specific ERMI values. The ERMI metric may be a useful tool to link the quantification of mold contamination in U.S. homes to some asthma health effects.
Published by Elsevier GmbH.

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1. Introduction

The prevalence of asthma continues to increase worldwide with about 334 million asthmatics currently (Asher and Pearce, 2014).

In the past 25 years, there have been hundreds of research articles and numerous review articles that have indicated that there was a qualitative link between water-damaged, moldy buildings and asthma (Quansah et al., 2012; Sharpe et al., 2015a). Governmental and international health organizations have also come to the same conclusion in their reviews of the scientific literature (IOM, 2004; WHO, 2009).

In previous studies, the association between mold exposures and asthma was only qualitative because there was no standardized

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http://dx.doi.org/10.1016/j.ijheh.2016.01.006
1438-4639/Published by Elsevier GmbH.

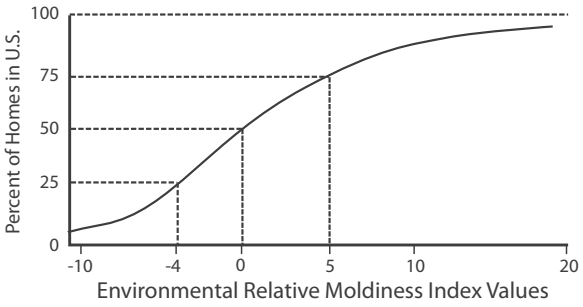

Fig. 1. The environmental relative moldiness scale is the assembled ERMI values (lowest to highest) from the American Health Homes Survey ($n = 1083$). The scale was then divided into quartiles. For example, 25% of homes have ERMI values <−4 and 25% have ERMI values >5.

sampling and analytical process for quantifying molds. Often the assessment was limited to a visual inspection or short air samples with many inherent limitations (Vesper, 2011). Our goal has been to turn this qualitative link between mold contamination and asthma into a quantitative assessment that can be acted upon.

To achieve this goal, a DNA-based method of mold identification and quantification called mold specific quantitative PCR (MSQPCR) was created (Haugland and Vesper, 2002). In order to interpret the data from the application of the MSQPCR technology, a standardized approach to sampling and analysis was required. This approach was produced as a result of the use of the MSQPCR technology in the Department of Housing and Urban Development's (HUD, 2010) 2006 American Healthy Homes Survey (AHHS) (Vesper et al., 2007; HUD, 2010). This survey included a national sampling of homes selected to represent the full range of conditions in the U.S. housing stock. The HUD AHHS utilized a living room and bedroom composite, settled-dust sample for the analysis of agents like lead, pesticides, mold, etc. A total of 1083 homes in the U.S. were sampled and EPA researchers obtained a portion of each dust sample for mold analysis.

The MSQPCR technology was used to identify and quantify 82 mold species in each of the AHHS samples. From this panel of 82 molds, 36 molds occurred in the samples at concentrations with a geometric mean of at least one cell per mg dust. From the analysis of these 36 molds in each sample and a mathematical treatment of the data, a relative moldiness scale called the environmental relative moldiness index (ERMI) was created (Fig. 1) (Vesper et al., 2007).

The 36 molds in the ERMI panel are considered "indicators," i.e. indicating water damage/dampness in the home (Table 1). The 26 Group 1 indicator molds were more common in water damaged homes and the ten Group 2 indicator molds were common in homes, even without water damage (Vesper et al., 2009; Vesper, 2011).

The ERMI value for each AHHS home was calculated, as shown in Eq. 1, by taking the sum of the logs of the concentrations of the 26 Group 1 species (s_1) and subtracting the sum of the logs of the concentrations of 10 Group 2 species (s_2) (Vesper et al., 2007). [The Group 2 molds are subtracted from the Goup1 molds to adjust for differences in cleaning habits, use of windows for ventilation, etc. (Vesper, 2011).]

$$\mathrm{ERMI} = \sum_{i=1}^{26} \log_{10}(s_{1i}) - \sum_{j=1}^{10} \log_{10}(s_{2j}) \quad (1)$$

To create the ERMI scale, i.e., the graphic representation of the data, each of the 1083 ERMI values from the AHHS survey were assembled from lowest to highest, as shown in Fig. 1. The resulting ERMI scale is a relative comparison of mold contamination in homes across the continental U.S.

Table 1
Environmental relative moldiness index (ERMI) indicator molds: Group 1 associated with water-damaged homes and Group 2 common in homes, independent of water damage.

Group 1	Group 2
Aspergillus flavus	*Acremonium strictum*
Aspergillus fumigatus	*Alternaria alternata*
Aspergillus niger	*Aspergillus ustus*
Aspergillus ochraceus	*Cladosporium cladosporioides* 1
Aspergillus penicillioides	*Cladosporium cladosporioides* 2
Aspergillus restrictus	*Cladosporium herbarum*
Aspergillus sclerotiorum	*Epicoccum nigrum*
Aspergillus sydowii	*Mucor* group
Aspergillus unguis	*Penicillium chrysogenum*
Aspergillus versicolor	*Rhizopus stolonifer*
Aureobasidium pullulans	
Chaetomium globosum	
Cladosporium sphaerospermum	
Eurotium amstelodami	
Paecilomyces variotii	
Penicillium brevicompactum	
Penicillium corylophilum	
Penicillium crustosum group	
Penicillium purpurogenum	
Penicillium spinulosum	
Penicillium variabile	
Scopulariopsis brevicaulis	
Scopulariopsis chartarum	
Stachybotrys chartarum	
Trichoderma viride	
Wallemia sebi	

For the sake of convenience, the ERMI scale is divided into quartiles (Fig. 1). For example, 25% of homes in the U.S. have an ERMI value below -4 and are in the lowest relative mold contamination quartile and the 25% of homes, with ERMI values above 5, are in the highest relative mold contamination quartile. Therefore, if the relative mold contamination of any home in the U.S. is sought, the ERMI provides a scale on which that home can be compared to the rest of the U.S. housing stock.

In this review article, six epidemiological studies, in cities across the U.S., will be summarized and the quantitative relationship between ERMI values and asthma described. Based on these six studies, the accuracy of the ERMI value's link to occupant asthma will be analyzed using receiver operating characteristic (ROC) curve and area under the curve (AUC) statistical analysis followed by a logistic regression analysis of the six studies to generate an equation that may be considered for use in predicting occupant asthma at specific ERMI values.

2. Support for the approach to the application of the ERMI metric

There have been many approaches to defining mold contamination. Most often indoor mold contamination is estimated by visual inspection. This approach ignores the fact that mold contamination can be hidden from sight and smell. Also, not everyone performing visual inspections is equally qualified. Therefore, the estimates are subjective and inspector dependent.

Sometimes short air samples (three to five minutes) are used to collect mold cells or spores which are then quantified by microscopic counting or by culturing on specific media. (Longer sampling times can result in too much density on the counting slide or Petri dish.) Short sampling times only provide information about what was in the air at that specific point in time. In addition, most mold spores cannot be identified to the species level and sometimes not even to the genus level, e.g., *Aspergillus* versus *Penicillium*, and vegetative mold cells or fragments cannot be identified at all by microscopic observations.